

AMENDMENTS TO THE SPECIFICATION

Kindly amend the title of the application as follows.

GENE THERAPY FOR ~~TUMOR~~ TUMORS USING MINUS-STRAND RNA
~~VIRUS VECTOR~~ VIRAL VECTORS ENCODING IMMUNOSTIMULATING
CYTOKINE IMMUNOSTIMULATORY CYTOKINES

Kindly insert the following heading and paragraph at page 1, line 5 of the English language specification.

Cross-Reference to Related Applications

This application is the U.S. National Stage of International Application No. PCT/JP2005/000238, filed January 12, 2005, which, in turn, claims the benefit of Japanese Patent Application No. 2004-005186, filed January 13, 2004.

Kindly amend the paragraph starting at page 4, line 29 of the English language specification as follows.

Fig. 3 shows MRI images of the whole 9L brain tumor treated with intracerebral administration of hIL2-SeV/ Δ M Δ F and subcutaneous immunization with irradiated 9L cells (T1-weighted image of a coronal plane after Gd-DTPA injection). ~~The Gd-DTPA enhanced tumor~~ The tumor in the Gd-DTPA-enhanced T1-weighted image is visualized as a white region. In three of the ten rats tested, established brain tumors, which were

detected three weeks after inoculation of tumor cells, were completely eliminated by week 4 with the combination therapy (Rat #3, Rat #5, and Rat #10).

Kindly amend the paragraph starting at page 4, line 35 of the English language specification as follows.

Fig. 4 shows an evaluation of the mean volume of 9L brain tumors based on Gd-DTPA-enhanced MRI three weeks after the inoculation of tumor cells. A combination of the administration of hIL2-SeV/ Δ M Δ F and subcutaneous immunization significantly reduced the volume ($86.5 \pm 63.8 \text{ mm}^3$, n=10) as compared with no treatment ($286 \pm 51.2 \text{ mm}^3$, n=10), the subcutaneous immunization alone ($197 \pm 48.9 \text{ mm}^3$, n=10), intracerebral administration of lacZ-SeV/ Δ M Δ F in combination with subcutaneous immunization ($233 \pm 73.2 \text{ mm}^3$, n=6), or intracerebral administration of hIL2-SeV/ Δ M Δ F alone ($256 \pm 53.2 \text{ mm}^3$, n=6). Each bar represents a “mean \pm S.E.”.

Kindly amend the paragraph starting at page 5, line 19 of the English language specification as follows.

Fig. 7 shows immunohistochemical analyses of the expression of CD4, CD8, and NK cell antigens in rats treated with intracerebral administration of lacZ-SeV/ Δ M Δ F and subcutaneous immunization with irradiated 9L cells (A), intracerebral administration of hIL2-SeV/ Δ M Δ F alone (B), and intracerebral administration of hIL2-SeV/ Δ M Δ F in

combination with subcutaneous immunization (C). (Magnification: x 200). The infiltration of CD4⁺ T cells and CD8⁺ T cells was more significantly detected in tumors treated with intracerebral administration of ~~SeV/IL-2~~ hIL2-SeV/ΔMΔF vector and subcutaneous immunization as compared with tumors that were subjected to the other treatments.

Kindly amend the paragraph starting at page 32, line 23 of the English language specification as follows.

Tumor-bearing rats were perfused through the ascending aorta with 4% paraformaldehyde. Brains were removed from the rats. 15-μm frozen sections from the brain samples were reacted with anti-CD4 eel (W3/25, Serotec, Oxford, UK), anti-CD8 eel (OX-8, Serotec), anti-NK cell (1.2.3, Serotec), and anti-human IL-2 (DAKO, Tokyo, Japan) monoclonal antibodies, and then reacted with a horseradish peroxidase-conjugated goat anti-mouse IgG (MBL, Nagoya, Japan). Then, the sections were stained with 3, 3'-diaminobenzidine tetrahydrochloride (Sigma, St. Louis, MI). The expression of β-galactosidase was detected by histochemical staining with X-Gal.

Kindly insert the sequence listing enclosed herewith at the end of the specification.